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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/375,605	08/17/1999	JAY M. SHORT	DIVER 1140-2	5334

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EXAMINER

NASHED, NASHAAT T

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 11/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.
09/375,605

Applicant(s)
Short, J. M.

Examiner
Nashaat T. Nashed

Art Unit
1652

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on Sep 9, 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 41-50 and 56-72 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 41-50 and 56-72 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
*See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 6) ☐ Other:

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on September 9, 2002 has been entered.

The after-final amendment filed April 15, 2002 and the amendment filed September 9, 2002 have been entered. Accordingly, Claims 51-55 have been canceled and claims 41, 46, 64, and 68 have been amended, and claims 71 and 72 have been entered.

Claims 41-50 and 56-72 are under consideration in this Office action.

New claim 72 contains multiple patentably distinct species. They are hydrolase, polyketide synthases, alkaline phosphatase, and β -glycosidase. Since the claims pending prior to the filing of RCE are drawn to polyketide synthase, claim 72 will be examined only to the extent required for the examination of the polyketide synthase subject matter.

The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: "at least 1 kb in size" in claim 44, "at least 5 kb in size" in claim 45, presumably "at least 10 kb in size" in claim 46, "at least 15 kb in size" in claim 47, "at least 20 kb in size" in claim 48, "at least 30 kb in size" in claim 49, "at least 35 kb in size" in claim 50 are not found in the original specification or the claims in the parent case, and therefore, it should be deleted.

In response to the above objection, applicant argue that claims 44-50 are fully supported by the specification in that the specification discloses that DNA up to 40 kb in size can be used in the claimed method, see for example, page 30, line 12 of the subject specification.

Applicants arguments filed 9/9/02 have been fully considered, but they are found unpersuasive. Contrary to the applicant's argument, page 30 does not contain the phrase "DNA up to 40 kb". Since the specification discussed any of these DNA fragments anywhere, it indicates that applicant has not intended to claim the subject matter at the time the application was filed.

New claim 72 is objected to under 37 CFR § 1.75(d)(1) as being in improper form because the claim states an improper Markush groups. Compounds included within a Markush group must "(1) share a common utility and (2) share a substantial structural feature disclosed as being essential to that utility." (See MPEP § 803.02.) The various members of the Markush group in the claims are different classes of chemical compound, i. e., enzymes having different catalytic activity, having different structure and indeed different function.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 41-50, and 56-72 are rejected under the judicially created doctrine of double patenting over claims 1-12 of U. S. Patent No. 5,939,250 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent for the reasons set forth in the prior Office action.

Claims 41-50, and 56-72 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 5,958,672 (672') in view of the prior art as exemplified by Arnold *et al.* (U. S. Patent 5,316,935) for the reasons set forth in the prior Office action.

Applicant has not filed a terminal disclaimer, but traverse the rejections stated above without giving any reason for the traversal of the rejection. Also, he indicates that a terminal disclaimer will be filed in the future.

The rejection will be obviated in the future when the terminal disclaimer is filed. New claims 71 and 72 are included in these rejections because they drawn to the same subject matter.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 41-50 and 56-72 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 41 is drawn to incomplete method because it is omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: (i) following step (a), isolating a DNA encoding a protein having a desired bioactivity; and (ii) need a step to isolate the wild-type protein of interest to compare the mutant protein to it.

In response to the above rejection, Applicant traverse the rejection on the ground that the claim could have more than one interpretation and cited the two possible interpretation of the claim in their view.

Applicants argument filed 9/9/02 have been fully considered, but they are found unpersuasive. The examiner agrees with the applicants that the missing steps in the claim indeed leads to a multiple interpretation of the claims and therefore, the claim is indefinite. Claims 42-50 and 56-72 are included in this rejection because they do not cure the deficiencies of the claim from which the depend.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 41-50 and 56-72 are rejected under 35 U.S.C. § 102(e) as being anticipated by Thompson *et al.* (U. S. P. 5,824,485)

In response to the above rejections, Applicant continues to argue that the claimed invention is not anticipate or obvious over Thompson *et al.* because the method taught by Thompson *et al.* is different from his.

Applicants' arguments filed 9/9/02 have been fully considered but they are not deemed to be persuasive. In traversing the rejection under 35 U. S. C. § 112, second paragraph, applicant indicates that there are two interpretation of the claimed method: (a) the gene library can be mutated as is prior to screening for the desired bioactivity or (b) a gene with desired enzymatic activity can be isolating and a mutant library is formed and screened for desired enzymatic activity. Keeping in mind interpretation (b) by the applicant of claim 41, lets consider the teachings of Thompson *et al.*

Thompson *et al.* teach method for screening molecular diversity by mixing and cloning genetic material from plurality of species of organism in a combinatorial gene library, see abstract and section 6, column 56 through 62. They teach that the genetic material can be obtained from any organism including those from environmental samples, plants and marine organisms to obtain antimicrobial, cancer or pharmaceutical compounds, see from column 12, line 35 through column 16, line 35. Also, they teach the preparation of the nucleic acid from donor organisms, see column 12, line 35 and section 5.3 starting in column 39, host cells see column 17, line 65, combinatorial expression libraries, see column 25, line 30, screening the combinatorial libraries, see column 32, line 58. The library can be constructed using any host cell such as the prokaryote *E. coli*, or the eukaryotic fungal cell such as yeast; or a multicellular organism, see section 5.1.3, starting on line 65, column 17. Thompson *et al.* specifically teach the isolation of nucleic acid sequence from soil or other mixed environmental samples (uncultured), see section 5.3.6, column 41, protocol for the construction of prokaryotic expression libraries and methods of screening the libraries, in particular for products of gene clusters such as secondary metabolites, see sections 5.4.1-5.4.14, columns 42-50, as well as methods for generating eukaryotic expression libraries using *E. coli*/*S. pombe* shuttle vector which would allow transferring the library from *E. coli* to *S. pombe*, section 5.5, columns 50-55. Finally, Thompson *et al.* teach and claim forming a chimeric gene library from genes of interests to develop diversity of gene clusters such as those of polyketides, see the entire document and claims 1-45. Chimeric gene cluster which have a desired activity anticipate claim 41 and its dependent claims 42-50 and 56-72. The gene cluster is isolate from a library constructed from a biological sample and subjected to mutation to produce a chimeric gene library which is screened for desired activity. Thus, Thompson *et al.* anticipate the claimed invention and therefore the claims remain rejected.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent

any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 41-50 and 56-72 are rejected under 35 U.S.C. § 103 as being unpatentable over Thompson *et al.* in view of the state of the art as exemplified by the cited art, Stemmer *et al.* (Stemmer *et al.* Proc. Natl. Acad. Sci. U. S. A. 1994, 91, 10747-10751) and Arnold *et al.* for the reasons set forth in the prior Office action, paper number 12.

In response to the above rejections, Applicant argues that there is no motivation to combine the reference and Thompson *et al.* motivation is directed to motivate one of ordinary skill in the art to do what Thompson *et al.* describe. Applicant further argues that there is no motivation in Thompson *et al.* to look to either Stemmer *et al.* or Arnold *et al.*

Applicants' arguments filed 9/9/02 have been fully considered but they are not deemed to be persuasive. Applicant appears to read the prior art in a selective manner. The main purpose of the teaching of Thompson *et al.*, Stemmer *et al.* and Arnold *et al.* are obtaining a diversified gene library. Thompson *et al.* teach a diversified gene library and isolating a gene encoding a desired activity following by mutation step to further diversify and obtain different desired activities. Both Arnold *et al.* and Stemmer *et al.* teach a method of obtaining a diversified mutant libraries. Certainly, the ordinary skill in the art would have been motivated to generate a diversified chimeric library by the teachings of both Arnold *et al.* and Stemmer *et al.* Stemmer *et al.* provide one of ordinary skill in the art with a motivation to develop a method of identifying a protein with modified activity by generate a heterologous population of DNA from a gene encoding an activity by mutagenesis, see column 4, lines 51-60. In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Finally as indicated above, one of the interpretation of the claimed invention according to the applicant made the claim anticipated by Thompson *et al.*, see the discussion above. Thus, Thompson still apply for the same reasons stated above. Since the one of ordinary skill has the teaching of the cited prior art, the motivation of the prior art, and the skills to carry out the claimed method, the claims remain rejected.

Claims 41-50 and 56-72 are rejected under 35 U.S.C. § 103 as being unpatentable over Radomski *et al.* (see IDS: U. S. Patent 5,849,491) in view of the state of the art as exemplified by the cited art, Thompson *et al.*, Stemmer *et al.* (Stemmer *et al.* Proc. Natl. Acad. Sci. U. S. A. 1994, 91, 10747-10751) and Arnold *et al.*

The teachings of Thompson *et al.*, Stemmer *et al.*, and Arnold *et al.* are summarized above.

Radomski teach a method of identifying a desired activity from an environmental sample. They teach a PCR amplification of DNA isolated from environmental sample and constructing a library, and screening the library for the desired activity, see column 4, line 3 through line 47 of column 5, and example 1-4.

Stemmer *et al.* provide one of ordinary skill in the art with a motivation to develop a method of identifying a protein with modified activity by generate a heterologous population of DNA from a gene encoding by mutagenesis, see column 4, lines 51-60. Thus, the ordinary skill in the art would have obtained an environmental sample, constructed a gene or cDNA library, screen for desired bioactivity, and isolate the DNA encoding the desired bioactivity as taught by Radomski, subjected the gene or DNA to one of several random mutation methods taught by Stemmer *et al.*, Thompson *et al.*, and Radomski, construct an expression library comprising the heterologous DNA population, and screen for the desired improved activity as taught by Stemmer *et al.* (claims 41-50, 56-72). Once a clone is identified having the DNA encoding the desired activity, the DNA can isolated by hybridization methods using a complementary sequence attached to as solid support. Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, clearly *prima facie* obvious.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nashaat T. Nashed, Ph. D. whose telephone number is (703) 305-6586. The examiner can normally be reached Monday, Tuesday, Thursday, and Friday from 9:00 a.m. to 5:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, can be reached on (703) 308-3804. The fax phone numbers for this Group are (703) 305-3014 and (703)308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.


Nashaat T. Nashed, Ph. D.
Primary Examiner